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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/680,742
Filing Date: October 06, 2003
Appellant(s): HAGSTROM ET AL.

Mark K. Johnson
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 4/27/2007 appealing from the Office action mailed April 5th 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

This appeal involves claim1, 2 and 4-14.

Claims 3 and 15-20 been canceled.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Concalves et al. "A Concise Peer Into the Background, Inital Thouhts and Practices of Human Gene Therapy" BioEssays, vol27, (2005), pp. 506-517

Verma et al. "Gene Therapy: Twenty-First Century Medicine" Annual Review of Biochemistry, vol74, (March 11,2005), pp. 711-738

Parekh-Olmedo et al. "Gene Therapy Progress and Prospects: Targeted Gene Repair" Gene Therapy, vol12, (2005), pp. 639-646

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2 and 4-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1, 2 and 4-14 are drawn to a process for delivering a polynucleotide to a prostate cell in a mammal comprising injecting a solution containing said polynucleotide into the lumen of a vessel, increasing permeability of the vessel to said polynucleotide, delivering said polynucleotide to the prostate cell outside of the vessel, and expressing said polynucleotide, and a process for expressing a gene in a prostate cell in vivo comprising injecting a solution containing a polynucleotide encoding said gene into the lumen of an afferent or efferent blood vessel of the prostate and delivering said polynucleotide to the prostate cell outside the vessel wherein said polynucleotide is expressed.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The breadth of the claims encompasses delivering a polynucleotide to a prostate cell in any mammal. This embodiment reads on gene therapy because the claimed process results in the expression of an exogenous polynucleotide in a target mammal even though no treatment is specified in the base claim of the instant application. The specification provides that the only intended use of the claimed invention is a method of gene therapy to treat disease, specifically, prostate cancer (pg. 1 lines 10-27, specifically, lines 20-22).

Whereas the nature of the invention is a process of delivery a transgene of interest to a prostate cell of a mammal, a review of the current art teaches that the field of gene therapy is unpredictable. At the time the invention was made, successful implementation of gene therapy protocols was not routinely obtainable by those skilled in the art. This is reflected by three reviews. Concalves (2005, BioEssays, Vol. 27, pgs. 506-517) teaches that with respect to gene therapy "one can conclude that further improvements in gene transfer technologies (e.g. control over transgene expression and integration) and deeper insights in host-vector interactions (e.g. knowledge on vector and gene-modified cell biodistribution following different routes of administration and the impact of innate and adaptive immunity) are warranted before clinical gene therapy reaches maturity" (pg. 514 col. 2 parag. 3). Specifically, Concalves teaches that gene therapy utilizing viruses has resulted in significant unpredictability, with retroviruses (pg. 513 col. 1 parag. 3 bridge col. 2 parag. 1), and adenoviruses (pg. 513, col. 2 parag. 2) providing only a fleeting success that was ultimately undone by a lack of transduction and low transgene expression levels. Parekh-Olmedo et al. teach (2005, Gene Therapy, Vol. 12, pgs. 639-646) with regard to gene repair utilizing gene therapy comprising single-stranded DNA oligonucleotides, repair of a gene of interest is again unpredictable. Specifically, successful gene repair has been reported in an animal model of severe kidney disease comprising carbonic anhydrase-deficiency utilizing a single-stranded DNA vector (pg. 641 col. 1 parag. 3). However, in a LacZ mouse model designed for testing gene repair using a variety of vectors, no correction of the mutant

LacZ gene was observed, resulting in the observation that delivery of DNA to a particular tissue continues to be a problem (pg. 641 col. 2 parag. 1). Verma et al. (2005, Annu. Rev. Biochem. Vol. 74, pgs. 711-738) teach that "the young field of gene therapy promises major medical progress toward a cure of a broad spectrum of human diseases from immunological disorders to heart disease and cancer. It has, therefore, generated great hopes and great hypes, but it has yet to deliver its promised potential" (pg. 732, parag, 2 lines 2-6). Verma et al. continues to teach that the process of gene delivery and expression is known as transduction, and that successful transduction requires overcoming a number of obstacles that are common to all vector systems (pg. 712, parag. 2 lines 1-3). Specifically, these obstacles include production of the vector, the targeting of the vector to a specified cell type, sustained gene expression, and avoidance of potential hazards such as insertional mutagenesis and immune responses (pg. 712, parag. 2 lines 3-19).

In view of the unpredictability of the art of gene therapy, a skilled artisan would require specific guidance in the instant disclosure to make and use the full scope of the claimed embodiment. Wherein the instant specification provides specific guidelines for delivering a polynucleotide to a prostate cell *in vivo*, the instant specification however, has not provided any relevant teachings, guidance, or working examples that teach or otherwise correlate to treating any disorder by expression of a transgene of interest in a prostate cell using the claimed processes. One of normal skill in the art would not be able to rely on the state of the art of *in vivo* gene therapy to transform a prostate cell *in vivo* with the claimed processes that would result in the treatment of any disease. Thus in view of the lack of guidance and direction provided by the specification for gene therapy in a prostate cell in any mammal, it would have required one of skill in the an undue experimentation to make and use the invention as claimed.

The working examples provided by the specification teach the delivery of a polynucleotide to the mouse prostate via injection of the dorsal vein of the penis (pg. 21, Example 1), via bladder injection (pg. 23, Example 2 lines 4-17), injection of tail vein (pg. 23, Example 2 lines 18-24), and injection of penis vein (pg. 24, lines 3-9). The specification continues to teach that delivery of polynucleotides to rat prostate was done via tail vein injection (pg. 29, Example 7). However, though the specification has taught that a polynucleotide can be delivered to a prostate cell in a mammal using the claimed process, the claims are examined in view of the intended use of the claimed invention, which is gene therapy. The art of record teaches that gene therapy is very unpredictable, and the instant specification fails to teach or address the limitations that encompass the treatment of any disease using gene therapy. Thus at the time of filing the skilled artisan would require an undue amount of experimentation without a predictable degree of success to make and use the claimed invention.

(10) Response to Argument

Applicant argues that the Examiner states that the claimed process encompasses gene therapy and though it may encompass other uses, gene therapy is one of these and is not fully enabled. Applicant argues that the Examiners position is that the specification provides that the only intended use for the claimed process is gene therapy. Applicant cites four specific passages of the specification to support the position that other intended uses exist in the specification for the claimed process. These passages are page 1 lines 25-27 (further biomedical research into the causes, mechanisms and potential treatments of enlarged prostate, prostate cancer and benign prostatic hyperplasia), page 2 lines 12-13 (process for the in vivo delivery of polynucleotides to prostate cells in a mammal), page 3 lines 29-30 and 33-44 (delivering a polynucleotide to a prostate cell for the purpose of altering the endogenous properties of the cell or to facilitate pharmaceutical drug discovery, drug target validation and research) and page 12 lines 15-19 (the polynucleotide of the claimed process whose presence or expression in a cell alters the expression or function of cellular gene, RNA or endogenous nucleotide sequence or to affect a specific physiological characteristic not associated with the cell prior to delivery of the polynucleotide). Applicant argues that the Examiner has contradicted himself regarding arguments over the intended uses of the claimed process during the Non-Final and Final Office actions and that he cannot dismiss his former reasoning without explanation. Applicant argues that that what is claimed is a process of delivery and expression in mammals and no more. That the claims are supported by numerous examples in the specification showing delivery and expression in mice, rats and monkeys. Applicant argues that no proof needs to be shown regarding a correlation existing between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor do they have to provide actual evidence of success in treating humans where such a utility is asserted. Applicant argues that the courts (Nelson v. Bolwer, 626 F.2d 853, 857, 206 USPQ 881, 884 (CCPA 1980)) have upheld that all that is required is a reasonable correlation between the activity and the asserted use. Applicant argues that gene therapy is not claimed, and that the Examiner on his own has stated that the Applicant has claimed gene therapy. Applicant argues that the term is very broad and Applicants' process certainly could be used in research toward therapy. Applicant concludes that the claimed process is enabled and that only reasonable adjustments to volume and pressure need be made for the process. These arguments are not persuasive.

At issue with the claimed process is the intended use. Given the broadest reasonable interpretation of the claimed process, this would include gene therapy. Applicant has argued that other uses exist for the claimed process other than gene therapy and has cited specific passages of the specification to support this line of reasoning. However Applicant is arguing from the position of claim 1 and its intended uses, however claim 1 is not the only claim rejected under 35 USC 112, first paragraph. The cited passages in Applicants arguments do not address all of the dependent rejected claims. Applicant is claiming a process for delivering DNA to a prostate cell in a mammal, however the dependent claims, particularly claims 13 and 14, point to treatment of prostatic cancer. Further dependant claim 9 claims that the DNA delivered by the claimed process induces an immune response. It is unclear why the skilled artisan would deliver DNA to a prostate cell in a mammal with benign prostatic hyperplasia or prostate cancer other than to treat said mammal. The term mammal obviously includes humans and the claims encompass humans suffering from prostatic cancer or its progenitor benign prostatic hyperplasia. While Applicant has chosen to use the term "process" for delivering DNA to a prostate cell in a mammal, the dependent claims would point to using the term "treatment" when they are given the broadest reasonable interpretation. Applicant has stated in their Appeal Brief that they have not claimed a gene therapy method, and that the Examiner has stated this on his own. However, the specification on page 1 lines 11-14 appears to contradict this statement. The subject matter of page 1 and page 2 lines 1-9 in the specification demonstrates the challenges to gene therapy and the delivery of polynucleotides that exists presently as the state of the art, and that beginning with Background of the Invention on page 2 of the specification Applicant teaches how their claimed invention will be an improvement of the current state of the art. There is a clear distinction that must be made here though. Using the term "gene therapy" implies that something is being treated and thus a higher bar is attributed because there is an expected outcome of treatment. Using the phrase "process of delivery" would imply that the bar is lower because the only requirement is that something, in this case polynucleotides, be delivered and that whether something is treated is not relevant. However, the claims demonstrate that there is no distinction between the two. Claims 1-8, 10 and 11 are vague in the sense that it is not understood why a polynucleotide is being delivered to a prostate cell in a mammal. Claim 9, 12 and 13 however clarify this question by teaching that the polynucleotide being delivered is for prostate cancer, and hopefully as a treatment option.

Applicants point to four areas in the specification that teach other uses for the claimed process:

The first of these areas is page 1 lines 25-27 (further biomedical research into the causes, mechanisms and potential treatments of enlarged prostate, prostate cancer and benign prostatic hyperplasia). The specification in this passage teaches that the claimed process will be used as a potential treatment for prostate cancer and is no different than the issues that have already been discussed of record regarding the unpredictability of gene therapy and treatment. There is no additional uses for the claimed process taught in this passage,

The second of these areas is page 2 lines 12-13 (process for the in vivo delivery of polynucleotides to prostate cells in a mammal). This passage is the scope of claim 1, and provides no additional uses that have not been addressed in the instant rejection of record. Essentially this passage is a restatement of claim 1,

The third area cited in the specification is page 3 lines 29-30 and 33-44 (delivering a polynucleotide to a prostate cell for the purpose of altering the endogenous properties of the cell or to facilitate pharmaceutical drug discovery, drug target validation and research). These intended uses for the claimed process are unclear. For altering the endogenous properties of the cell, the skilled artisan could reasonably conclude that this is for some beneficial effect of the cell that would result in treatment. If the process is used to facilitate pharmaceutical drug discovery, drug validation and research the skilled artisan must ask why and what is being delivered to a prostate cell? Drug discovery and drug target validation for what? A potential therapeutic nucleic acid to be delivered to the prostate cell? If a drug is being screened using the claimed method then that drug must have some intended use to treat something. In the instant case it can be inferred by the skilled artisan based upon the specification that the target is a cancerous prostate cell, and that a potential drug (therapeutic nucleic acid) is being screened. Essentially again, a treatment method,

The fourth area cited is page 12 lines 15-19 (the polynucleotide of the claimed process whose presence or expression in a cell alters the expression or function of cellular gene, RNA or endogenous nucleotide sequence or to affect a specific physiological characteristic not associated with the cell prior to delivery of the polynucleotide). This use for the claimed process appears no different than a treatment method. If the skilled artisan is going to use the claimed process to alter the expression or function of a cellular gene, RNA or endogenous nucleotide sequence to affect a specific physiological characteristic not associated with the cell prior to delivery of a nucleic acid then the intended use is not clear outside of treatment. Cancerous cells have aberrant cellular processing that impacts cellular division and apoptosis and is a hallmark of all cancer cells. To modify a specific physiological characteristic that was not present prior to the delivery of a nucleic acid i.e. apoptosis, could again be reasonably construed by the skilled artisan as a treatment method.

The use of the term "gene therapy" appears to be the point of contention in the prosecution history of the instant application. Applicants have argued that this is not the only use for the claimed invention and pointed to passages in the specification that would teach other uses. The pending rejection is over all of the claims and is made when the claims are given their broadest reasonable interpretation, which by the Examiners account, includes gene therapy as a treatment option for prostate cancer. Applicants have argued that other uses exist for the claimed process, however a detailed examination of these other intended uses cited by Applicant does not provide the skilled artisan with any specific use outside of a potential treatment of prostate cancer or pre-cancerous prostate cells. Thus the skilled artisan would require and undue amount of experimentation without a predictable degree of success to make and use the claimed process. Applicants have argued that *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881 (CCPA 1980) provides that Applicants do not have to prove that a correlation exists between a particular activity and an asserted therapeutic use. While this has been demonstrated in the courts, that is not the issue in the instant case. Applicant has not asserted any therapeutic use for the process in the claims, however the specification is relied upon to provide that the claimed process will be used as a method of treatment. The rejection of record does not question the absence of providing any treatment in humans with the claimed process, rather the rejection addresses whether any treatment using the claimed process will work at all.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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